Notice of Allowability	Application No.	Applicant(s)	
	10/556,454	VOLLMER, TIMOTHY	
	Examiner	Art Unit	
	MAURY AUDET	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the 12/20/10 Advisory Action, Withdrawn*.

2. ☒ The allowed claim(s) is/are *2,3,6,23,27,28 and 31*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *2/11/11* .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/Maury Audet/
Primary Examiner, Art Unit 1654

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Gary Gershick, Applicant's Representative on 2/11/11.

IN THE CLAIMS

In claims 2, 3, 6, 27 and 28, line 1, the numeral "1" has been deleted, and the numeral --31-- inserted.

Claim 23, after the last term "subject", the following phrase has been inserted:

$12\ mg/m^2$

--, comprising administering to the subject 3 doses of

of mitoxantrone by intravenous infusion, at months 0, 1, and 2; followed 2 weeks later by daily subcutaneous injection of 20 mg glatiramer acetate, for at least 6 weeks--.

Claim 31 has been deleted, and replaced in it's entirety to now read:

A method of treating a subject afflicted with a form of multiple sclerosis

$12\ mg/m^2$

comprising administering to the subject 3 doses of
of mitoxantrone by intravenous infusion, at months 0, 1, and 2; followed 2 weeks later by daily subcutaneous injection of 20 mg glatiramer acetate, for at least 6 weeks.

Claims 1, 4, 7-13, 19-21, 24-25, and 29-30 have been cancelled without prejudice.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance:

A method of treating multiple sclerosis (MS) comprising the amended limitations (exact test protocol) of claim 31 (above; mitoxantrone (immunosuppressant) with glatiramer acetate (GA; immunomodulator); two different classes of MS drugs) and a package requiring all the limitations of claim 31, was not found to be reasonably taught or suggested by the prior art of record.

Mitoxantrone was found to be combined/sequentially administered with methylprednisone, another immunosuppressant for the rapidly progressing form MS. But not expressly with any other MS drugs. While GA was found/suggested to be used with a number of other immunomodulators/other MS drugs, primary for the relapsing remitting form of MS. Thus, since mitoxantrone and GA were not expressly combined together, in an enabling disclosure, no anticipatory reference was found that read on the presently claimed invention.

However, since both mitoxantone and glatiramer acetate are well known for treating MS, the Examiner raised the In re Kerkhoven type issue/rejection under 35 USC 103 (obvious to combine two known compounds for their known purpose).

Although there are many MS drug combinations/sequential regimens that have been found enabled and advantageous such as e.g. the two immunosuppresants mitoxantrone and methylprednisone); the literature taught that the combination of e.g. methylprednisone (immunosuppressant) with interferon beta-1a (immunomodulator), did not seem to affect disability progression of MS any more than IFB-1a alone, in the patients tested. Thus, the art teaches that combinations/sequential regimens of two known MS drugs are not necessarily

efficacious and could even be harmful (due to the different side effects, some long-term, that all the MS drugs can cause). [Which is further supported by the FDA's stance that combinations of known drugs for the same use are not necessarily predictable].

However, Applicant did find that the presently claimed sequential administration combination of mitoxantrone with GA produced better effects than GA alone, and therefore presented unexpected results over what the art could predict, without testing.

Thus, although the art is filled with other teachings of combinations/sequential regimens of various drug combinations/sequential regimens of other MS drugs (namely recently advanced drugs within the last 20 years roughly), there was not a teaching/suggestions of combining/sequentially administering mitoxantrone and GA, including all the limitations of claim 31. Therefore, the invention as claimed by amendment, is not found to be reasonably taught or suggested by the prior art of record, or sustainable under an In re Kerkhoven type fact pattern and is hereby allowed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 2/14/2011

/Maury Audet/
Primary Examiner, Art Unit 1654